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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/245,615	02/04/1999	JAMES P. HOEFFLER	INVIT1100-1	5087

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/245,615	HOEFFLER ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION. .

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-37,39,40,51,52,54-56 and 58-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-37,39,40,51,52,54-56 and 58-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/09/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's response to the Office Action mailed 13 October 2004 is acknowledged. In amendment-A filed therein claims 31, 37, 39-40, 52, 55-56, and 58-59 were modified. New claims 60-65 were added and claims 1-30, 38, 41-50, 53 and 57 were cancelled.

2. Currently claims 31-37, 39-40, 51-52, 54-56 and 58-65 are pending and under consideration.

3. Objections and/or rejections of record not reiterated below have been withdrawn.

OBJECTIONS MAINTANED

Drawings

4. The drawings in this application are objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948). Applicant is required to submit a proposed drawing correction in reply to this office action. However, formal correction of the noted defect can be deferred until the examiner allows the application.

Applicant has requested that the formal drawings submitted with Applicant's amendment mailed July 2, 2003 in continuation US Serial No. 10/035,368 be utilized for the instant application.

If the drawings were changed and approved during the prosecution of the prior application, a petition may be filed under 37 CFR 1.182 requesting the transfer of such drawings, provided the parent application has been abandoned.

However, a copy of the drawings as originally filed must be included in the 37 CFR 1.60 application papers to indicate the original content. An approved petition regarding the utility of the drawings in US Serial No.10/035,368 has not been filed. Accordingly the objection is maintained.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 31-37, 39-40, 51-52, 54-56 and 58-65 are rejected under 35 U.S.C. 1 12, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The term "uncharacterized" in claims 31 and 37 is a relative term, which renders the claim indefinite. The term "uncharacterized" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree', and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to what applicant intends to encompass with respect to the antibodies (what makes them uncharacterized – unknown binding affinity).Are uncharacterized antibodies directed to any known antibody or unknown antibodies? Are "uncharacterized antibodies" defining the binding ability of the antibody? For example it is not known what antigen binds the antibodies? Or does "uncharacterized" mean the antibodies are to meet some other parameter not clearly identified.

It is suggested that the term be removed or defined such that the intended meaning is clear. Please clarify.

Response to Argument

Applicant contends that the skilled artisan would know that "uncharacterized" antibodies would mean antibodies that are not characterized, for example with respect to antigen binding and/or affinity. This argument was carefully considered but not found persuasive because the "uncharacterized" is not defined and therefore encompasses an infinite possible readings. This renders the claims indefinite. The rejection is maintained.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 37, 55, 56, 58, 59, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65).

Shalon et al. teach microarrays with immobilized reagents. The immobilized reagents include antibodies and antibody fragments that are dispensed on selected array positions. See abstract, page 11 lines 15-24, and page 31 lines 32-35, for example.

The discrete positions on the microarray are spaced apart (spatially addressable) on the solid support. See page 5 line 33, page 6 line 2, page 7 line 26-27. The source (cell line or cell type) of the antibodies at each discrete location is known (claim 55). See page 12 line 32 through page 13 line 2.

In one embodiment the microarray is treated to reduce non-specific binding with a polycationic polymer. See page 7 lines 30-32. The microarray has reagents (antibodies) spotted in discrete positions between 0.01 nanoliters and 100 nanoliters. See page 6 lines 8-10. The microarray also comprises regions from 100 locations per square centimeter to 1000 locations per square centimeter (reading on claim 64). Page 12 lines 3-9.

Shalon et al. differ from the instant invention in not specifically teaching uncharacterized antibodies.

However, Stevenson et al. disclose ELISA procedures involving uncharacterized antibodies. See abstract and page 63 2nd column, 2nd paragraph.

Specifically, uncharacterized antibodies to collagen IV are shown to be elevated in basement membrane damage. See page 64 - Discussion.

The increased serum levels of less characterized (uncharacterized) antibodies may be useful in determining antibody-mediated diseases and basement membrane disturbances. See page 63 1st column last lines through 2nd column lines 7.

It would have been obvious to one of ordinary skill in the art to employ uncharacterized antibodies as taught by Stevenson et al. in the microarray of Shalon et al. because Stevenson et al. taught that uncharacterized antibodies were useful in measuring basement membrane disturbances or damage and subsequent antibody-mediated diseases. See Stevenson et al. page 63 1st column last paragraph through column 2.

II. Claims 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) as applied to claims 37, 55, 58, 59, 63 and 64 above, and further in view of Ragg and Whitlow (FASEB, Vol.9, January 1995, pages 73-80).

Please see previous discussion of Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) as set forth above.

Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, pages 63-65) differ from the instant invention in not teaching antibody fragments such as single chain/stranded recombinant antibody compositions.

However, Raag and Whitlow disclose single chain recombinant antibody fragments (sFv) consisting of only the variable light chain (VL) and variable heavy chain (VH) domains covalently linked by a polypeptide linker.

Because the single chain recombinant antibody fragments are small they have rapid pharmacokinetics and tumor penetration in vivo. See abstract. These single chain recombinant antibody fragments are derived from the antigen-binding domain of antibodies and are useful in any molecular recognition or binding application. See page 74 2nd column 2nd paragraph.

SFv's are disclosed as tine reducers in ELISA applications. See page 74 2nd column middle of the 3rd paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use antibody fragments like recombinant single chain/stranded antibodies (sFv) as taught by Raag and Whitlow in the microarray of Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) to produce arrays to perform multiple sample analysis in the rapid detection systems because Raag and Whitlow taught that sFv's were small allowing for rapid penetration (abstract), useful in any antibody application (page 74 2nd column 2nd paragraph), and reduced time in ELISA procedures page 74 2nd column middle of the 3rd paragraph.

III. Claim 65 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and further in view of Kohler et al. (Nature, 256, August 7, 1975, pages 495-497).

Please see previous discussion of Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) as set forth above.

Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) differ from the instant invention in not teaching that the source of the antibodies is from a known hybridoma cell line.

However, Kohler et al. teach antibody production from a known hybridoma cell (tissue culture cell lines made from fused myeloma and spleen cells from an immunized donor). Kohler et al. disclose that the production of antibodies via hybridoma is a satisfactory source of monoclonal antibodies of predefined specificity.

The cells are versatile allowing for antibody production from different origins, can be grown in massive quantity, provide specific antibodies, and could prove valuable for medical and industrial utility. Page 495 1st paragraph and page 497 2nd column last paragraph. The specification teaches that the reference of Kohler et al. teaches hybridoma procedures on page 8 lines 13-19.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize hybridoma cells to produce antibodies as taught by Kohler et al. in the antibody microarray of Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) because Kohler et al. taught that hybridoma cells are versatile allowing for antibody production from different origins, can be grown in massive quantity, provide specific antibodies, and could prove valuable for medical and industrial utility. Page 495 1st paragraph and page 497 2nd column last paragraph.

IV. Claims 31-33, 36, 51-52, 54 and 60-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and further in view of Foster et al. (U.S.Patent#4,444,879).

Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) is set forth above. Specifically, Shalon et al. disclose antibodies immobilized on microarrays while Stevenson et al. teach the utility of uncharacterized antibodies.

However, the references fail to teach the reagents as a kit. Kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a microplate, positive controls, negative controls, standards, and instructions are taught. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay microarry and reagents as taught by Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and format them into a kit because Foster et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay.

V. Claims 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and further in view of Foster et al. (U.S.Patent#4,444,879) as applied to claims 31-33, 36, 51-52, 54 and 60-61 above, and further in view of Ragg and Whitlow (FASEB, Vol.9, January 1995, pages 73-80).

Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and further in view of Foster et al. (U.S.Patent#4,444,879) is set forth above.

Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and further in view of Foster et al. (U.S.Patent#4,444,879) differ from the instant invention in not teaching antibody fragments such as single chain/stranded recombinant antibody compositions.

However, Raag and Whitlow disclose single chain recombinant antibody fragments (sFv) consisting of only the variable light chain (VL) and variable heavy chain (VH) domains covalently linked by a polypeptide linker.

Because the single chain recombinant antibody fragments are small they have rapid pharmacokinetics and tumor penetration in vivo. See abstract. These single chain recombinant antibody fragments are derived from the antigen-binding domain of antibodies and are useful in any molecular recognition or binding application. See page 74 2nd column 2nd paragraph.

SFv's are disclosed as tine reducers in ELISA applications. See page 74 2nd column middle of the 3rd paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use antibody fragments like recombinant single chain/stranded antibodies (sFv) as taught by Raag and Whitlow in the microarray of Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and further in view of Foster et al. (U.S.Patent#4,444,879) to produce arrays to perform multiple sample analysis in the rapid detection systems because Raag and Whitlow taught that sFv's were small allowing for rapid penetration (abstract), useful in any antibody application (page 74 2nd column 2nd paragraph), and reduced time in ELISA procedures page 74 2nd column middle of the 3rd paragraph.

VI. Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and further in view of Foster et al. (U.S.Patent#4,444,879) as applied to claims 31-33, 36, 51-52, 54 and 60-61 above, and further in view of Kohler et al. (Nature, 256, August 7, 1975, pages 495-497).

Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and further in view of Foster et al. (U.S.Patent#4,444,879) is set forth above.

Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and further in view of Foster et al. (U.S.Patent#4,444,879) differ from the from the instant invention in not teaching that the source of the antibodies is from a known hybridoma cell line.

However, Kohler et al. teach antibody production from a known hybridoma cell (tissue culture cell lines made from fused myeloma and spleen cells from an immunized donor). Kohler et al. disclose that the production of antibodies via hybridoma is a satisfactory source of monoclonal antibodies of predefined specificity.

The cells are versatile allowing for antibody production from different origins, can be grown in massive quantity, provide specific antibodies, and could prove valuable for medical and industrial utility. Page 495 1st paragraph and page 497 2nd column last paragraph. The specification teaches that the reference of Kohler et al. teaches hybridoma procedures on page 8 lines 13-19.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize hybridoma cells to produce antibodies as taught by Kohler et al. in the antibody microarray of Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) and further in view of Foster et al. (U.S.Patent#4,444,879) because Kohler et al. taught that hybridoma cells are versatile allowing for antibody production from different origins, can be grown in massive quantity, provide specific antibodies, and could prove valuable for medical and industrial utility. Page 495 1st paragraph and page 497 2nd column last paragraph.

Response to Arguments

Applicants contend that the amended claims reading on a microarray with uncharacterized antibodies immobilized thereon, is not anticipated by the patent of Hirschfeld (US Patent #4,514,508). This argument was carefully considered and found persuasive. Accordingly, the reference combination of Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) under 35 USC 103(a) has been cited to make the claimed invention obvious. Arguments directed to Hirschfeld are MOOT because the reference has been withdrawn.

Applicants argues that the reference of Raag et al. and Heller et al. do not provide the teaching that is missing in Hirschfeld. This argument was carefully considered but not found persuasive because a deficiency in a reference is not overcome by pointing out that a reference lacks a teaching for which other references are relied. In re Lyons, 364 F.2d 1005, 150 USPQ 741, 746 (CCPA 1966). Specifically, Shalon et al. (WO 95/35505) in view of Stevenson et al. (Biomarkers, 1997, 2, 63-65) have been cited for the limitations missing in Hirschfeld.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., Heller do not describe methods or data for making or using microelectronic device containing protein arrays) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The instant claims are directed to microarrays and kits containing them. The methods of making them are not recited.

Remarks

7. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187) disclose enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186.

8. For reasons aforementioned, no claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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